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MISMATCH NEGATIVITY (MMN) INDEXES SUBCLINICAL NEUROLOGICAL DIFFERENCES IN HIV PATIENTS DURING RAPID PERCEPTUAL PROCESSING

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Summary

Thirteen asymptomatic HIV-infected (HIV+) and 13 healthy control (HIV-) subjects were instructed to detect "oddball" target tones from among a sequence of nontarget tones delivered rapidly (3 tones/sec) in one ear while ignoring a similar sequence delivered simultaneously in the opposite ear. Event-related potentials (ERPs) to all stimuli were recorded from midline scalp sites. Both groups produced ERP correlates, termed the mismatch negativity (MMN), to the oddball tones during delivery. However, the HIV+ group produced MMNs that were different in morphology to the HIV- group, suggesting that HIV may alter attentional perceptual processing. These results suggested that auditory ERPs elicited by rapid, dichotic stimulus presentations may be useful tools in monitoring subclinical effects of HIV-related neuropathology on perceptual processing.

INTRODUCTION

Recent reports about the pathogenesis of the human immunodeficiency virus (HIV) challenge the widely accepted concept of latency in the early stages [1-2]. In fact, viral replication is a constant feature following established infection [1-2]. It is now also appreciated that symptomatic central nervous system (CNS) involvement occurs in at least 60% of HIV infected individuals [3]. Apparently, infected macrophage cells function as vectors in transmitting HIV-infected particles [4-6], and further contribute to CNS pathology by secreting neurotoxic substances (e.g., elevated cytokines [5]). Whether these underlying neurological complications produce detectable cognitive impairment in the early stages of the disease remain poorly understood, since often times patients appear to be neurologically normal as assessed by neuropsychological tests [7-8].

Nevertheless, some experts [9-14] report cognitive impairment in a percentage of HIV-infected (HIV+) asymptomatic subjects on several neuropsychological tasks that required speed of information processing, verbal memory, psychomotor speed, and attention, while others report no impairment [15-19]. This disparity suggests that either most HIV+ individuals do not become impaired until they are in a more advanced stage of HIV infection, or that some neuropsychological measures may be insensitive to subtle changes in cognitive function until neuropathology is so extensive that cognition and behavior are more dramatically affected.

To evaluate HIV-related, neuropsychological abnormalities, Linnville, Elliott, and Larson [20] tested a small (N = 13) group of dated, HIV seroconverters (HIV+) and compared them to a small (N = 13) group of healthy, uninfected (HIV-) individuals over several performance measures. Brain-emitted event-related potentials (ERPs) were recorded from them while detecting auditory "oddball" targets in rapid (3 tones/sec) delivery, of dual-channel (i.e., dichotic) sequences of tones. Reaction time and number of "hits" were also recorded from them during this assessment. Behavioral measures that tested intelligence, computational skills, visual-spatial memory, and psychomotor ability were also used and the results compared to several normative databases. The behavioral results indicated that the HIV+ group performed similarly to the HIV- group. Also, both groups performed similarly (about 50% "hits" in about a 450-ms response time) in detecting oddball targets in the dual oddball task. The ERP results however, indicated that the HIV+ group produced attenuated P300s (an ERP positive peak at about 300 ms) to detected oddball tones. This suggested some form of underlying neurological changes to rapid, cognitive decision-making in individuals who had HIV for periods ranging from three months to eight years. Thus, the auditory ERPs elicited by rapid, dichotic stimulus presentations were

more sensitive to subclinical effects of HIV-related neuropathology than conventional behavioral measures. Furthermore, the results demonstrated that the auditory dual oddball task may be a useful tool in monitoring the progression of HIV-related neuropathology.

The MMN

An associated phenomenon to that involved in the elicitation of the P300, is known as the "mismatch negativity" (MMN; [21-24]). It is produced during the dual oddball task, and may also be useful in monitoring HIV-related neuropathology.

When subjects hear an occasional, acoustically-different tone delivered among a sequence of standard tones, a cerebral response to the difference is induced. A negative component in the 100 ms to 200 ms region of the ERP termed the MMN is thought to index responses in an acoustical, sensory feature analysis system to the acoustical deviancy of the infrequent, oddball tones [21]. Näätänen and Picton [21] reported that the greater the difference in frequency between oddball tones and standard tones, the larger the amplitude of the MMN and the earlier it was elicited. Näätänen postulated that the MMN is an automatic feature analysis response, and therefore, was independent of any attentional influence [21-24]. However, his hypothesis was derived from presenting dual oddball tone sequences dichotically at fairly slow interstimulus intervals (ISI) (i.e., 800-ms ISI [22-23]). Woldorff, Hackley, and Hillyard [25] considered this a long enough period to allow attention to become an important element in the acoustical feature analysis of stimuli in the "ignored" channel of input. To test Näätänen's hypothesis, Woldorff optimized attentional focus by presenting rapid (about 3 tones/sec), dual-oddball sequences of tones to subjects. They were instructed to focus attention to one ear and detect occasional "softer" (approximately 40 dB SL) oddball tones from among tones that were identical in frequency but "louder" (55dB SL) in intensity and to ignore a similar sequence delivered in the opposite ear. Woldorff et al. [25] reported that an attentional system was responsible for augmenting the amplitude of the MMN elicited to oddball tones in the attended ear and also was responsible for suppressing the amplitude of the MMN elicited to oddball tones in the ignored ear. Consequently, their findings suggested an attentional system that could gate early sensory information processing.

Our earlier study [20] employed a paradigm similar to that of Woldorff et al. [25]. The current report, focusing on MMN activity elicited prior to the production of the P300 component, is a re-examination of data from the study reported earlier [20]. The purpose is to determine whether the MMN, a different phenomenon from the P300, is suppressed in the HIV group. This would be indicative of underlying neurological changes affecting perceptual processing and target detection [20].

METHODS

Subjects

Thirteen asymptomatic HIV-seropositive (HIV+) males and 13 normal, healthy control HIV seronegative (HIV-) males were tested. The 13 HIV-infected males had an estimated mean duration of infection of 3.6 years (Table 1). All subjects had normal intelligence (based upon normative data, and pre- and post-infection scores from the Armed Services Vocational Assessment Battery), good hearing, normal body temperature, and were free from depression and anxiety (Spielberger State-Trait Anxiety Inventory [26] and the Beck Depression Inventory [27]). These characteristics were described in further detail in Linnville et al. [20].

Table 1. Demographic information.

HIV Subjects								Control Subjects		
Subj	Race[a]	Age	HIV+	HIV-	T4	Stage[b]	AZT	Race[a]	Age	ELISA[c]
1	CA	22	3/93	9/91	360	III	YES	CA	35	HIV-
2	CA	31	7/91	7/89	580	I	NO	CA	30	HIV-
3	AA	30	6/93	10/91	320	V	NO	CA	30	HIV-
4	CA	30	2/88	5/86	700	I	YES	CA	31	HIV-
5	CA	29	7/88	2/88	550	II	NO	CA	29	HIV-
6	CA	24	5/92	7/91	650	I	NO	CA	30	HIV-
7	AA	34	4/87	7/86	690	II	NO	CA	33	HIV-
8	AA	41	7/93	2/92	210	IV	YES	CA	20	HIV-
9	AI	30	8/92	9/91	690	I	NO	HI	41	HIV-
10	HI	32	9/93	9/92	440	II	YES	CA	32	HIV-
11	CA	21	7/93	4/93	780	I	NO	CA	26	HIV-
12	CA	25	9/88	12/85	430	I	NO	CA	22	HIV-
13	CA	33	5/86	?	640	II	YES	CA	24	HIV-
Means		29.4			542				29.5	
SD		±5.4			±174				±5.6	

[a] CA = Caucasian, AA = African American, AI = American Indian, and HI = Hispanic
[b] Walter Reed Staging Classification.
[c] ELISA = enzyme-linked immnunoabsorbant assay

Several HIV+ subjects were being treated with zidovudine (AZT), including one individual (HIV+ Subject No. 8) who nearly met AIDS criteria. Reports indicate that this antiretroviral treatment improves CD4+ T-cell counts, at least temporarily [28], reduces the frequency of diffuse demyelinating lesions of the cerebral white matter [29], and indirectly

improves a range of cognitive functions (i.e., attention, memory, motor skills, and general mental speed [30]). Furthermore, a post hoc series of stepwise discriminant analyses of the data failed to identify distinct AZT and nonAZT subgroups within the HIV+ group's data set. Thus, the HIV+ subjects were a relatively healthy group and all were asymptomatic for any opportunistic diseases.

Stimuli And Task

A dual-oddball, selective-attention task was used similar to one reported by Woldorff et al. [25]. Stimuli consisted of a sequence of 1000-Hz tone pips presented to the left ear, interspersed with a sequence of 3150 Hz tone pips presented to the right ear. Tones were brief (14 ms), presented at approximately 3 tones per second (i.e., ISI 131 - 305 ms), and alternated between the two ears. Five percent of the tones in each ear were soft-intensity "targets" (70 dB SPL) and 95 percent in each ear were relatively louder "nontargets" (85 dB SPL). Subjects attended to only one designated ear and pressed a button in response to targets detected in that ear while ignoring deliveries in the other ear. Each run consisted of 313 loud and 17 soft tone pips per ear, delivered in a semirandom order. The "attended" ear was alternated, with 4 runs per ear.

ERP Recording Procedure

ERPs were recorded at frontal (Fz), central (Cz) and parietal (Pz) scalp sites using the Ten-Twenty International electrode placement system [31], with a left-ear reference. Eye movements were also recorded with electrodes at supraorbital and outer canthus positions of the left eye and were later used for rejecting data that contained eye artifact. Impedances of all electrodes were below 5 kΩ. Signal frequency bandwidths were set between 0.1 Hz to 100 Hz and amplification was set at 20,000 times. The signals were digitized online at a sampling rate of 256 Hz and stored on optical disks for off-line analysis. Auditory stimuli were delivered via ear-insert stereophones from a separate computer linked to the data acquisition computer. Button presses were "marked" onto the ERP signals collected for off-line analyses. The recording procedures were explained more fully in Linnville et al. [20].

Data Analyses

For the current analyses, an ERP epoch consisted of a 200-ms prestimulus baseline followed by a 400-ms poststimulus period. Artifact-free, normalized (relative to the prestimulus baseline period) epochs were averaged together according to stimulus type to yield an average ERP for each condition. An averaged ERP to nontarget stimuli consisted of approximately 2,504 single trials (313 trials x 4 runs x 2 ears attended to) and an averaged "hits-only" target ERP consisted of approximately 136 single trials (17 trials x 4 runs x 2 ears attended to).

ERP mean amplitudes (i.e., the average amplitude for ERP data within a temporal period) for three successive 50-ms periods (Window A= 100-150 ms, Window B= 150-200 ms, and Window C= 200-250 ms) were calculated relative to the 200-ms prestimulus baseline. These latency windows were chosen for the statistical analyses so that the results could be compared to the findings in Woldorff et al. [25]. Each set of mean amplitudes were subjected to a series of analyses of variance (ANOVA) using a Group (2) x electrode Sites (3) x Tone-type (2; target vs. nontarget) repeated measures, mixed-factor design with the latter two variables being the repeated measure. The "attend" mean amplitude measures were analyzed separately from the "ignore" mean amplitude measures in order to specifically test for group differences in the MMN (i.e., target vs. nontarget). Thus, the "attention effect" (i.e., attend target vs. ignore target) which is reported in Linnville et al. [20], is not discussed here. In order to evaluate the MMN in more detail, MMN difference waveforms (i.e., attend MMN difference waveforms = attend target minus attend nontarget; ignore MMN difference waveforms = ignore target minus ignore nontarget) were calculated using the same latency windows. Mean amplitude measures from the MMN difference waveforms were computed and subjected to a series of separate ANOVAs using a Group (2) x electrode Sites (3) x Attention (2) repeated measures, mixed-factor design with the latter two variables being the repeated measure. The Geisser-Greenhouse correction to the degrees of freedom was used for those analyses that had more than two levels in any factor in order to avoid a biased F test with the repeated measures design [32]. The t-test "critical difference between means" procedure for planned pairwise comparisons was used to confirm the direction of any interactions and to avoid cumulative type I error during multiple comparisons [33].

RESULTS

Figure 1 (top panel) shows the ERPs for the HIV+ group (left column) and the HIV- group (right column) elicited at the central (Cz) scalp site by the target tones when they were attended (first row) and ignored (second row), superimposed upon ERPs elicited to the corresponding nontarget tones. In both groups, a negative deflection is evident in the target ERPs relative to the nontarget ERPs. This is the MMN wave which began around 100 ms poststimulus, lasted about 300 ms, and was followed by a large P300 response (at approximately 300-400 ms).

Figure 1 (bottom panel) also shows the MMN difference waves which show more clearly the variance in the comparison between the ERPs elicited by the target versus nontarget tones

(top panel). The HIV+ group demonstrates a broad positivity in the region of 100 to 150 ms, and a bifarcated negativity in the region of 150 ms to 250 ms compared to the HIV- group MMN.

Grand mean amplitudes of the ERPs are displayed in Table 2, and the corresponding grand mean amplitude measures from the computed MMN difference waveforms are displayed in Table 3. The ANOVA results of the ERP mean amplitude measures and the computed MMN difference waveforms are displayed in Tables 4 and 5, respectively. Only significant group differences are reported below in detail.

ERP Results

Window A (100-150 ms). The analysis of mean amplitude measures from the "Attend" condition in Window A produced a main effect for Group and a main effect for electrode Site. The Group main effect indicated a greater negativity in the mean amplitude measures in this latency window for the HIV- group in comparison to the HIV+ group (Table 2). Figure 1 (top panel) shows that the HIV- group (right column) produced N100 components in Window A during the Attend condition for both target and nontarget tones. By comparison, the HIV+ group (left column) produced an N100 component to attended nontargets but did not produce an N100 component to attended targets in this latency window. A negative "spike" component does appear near 200 ms during the Attend condition that may be a shifted N100 component. The ANOVA of the mean amplitude measures from the "Ignore" condition in this latency window resulted in only a main effect for electrode Sites that is noted in Table 4.

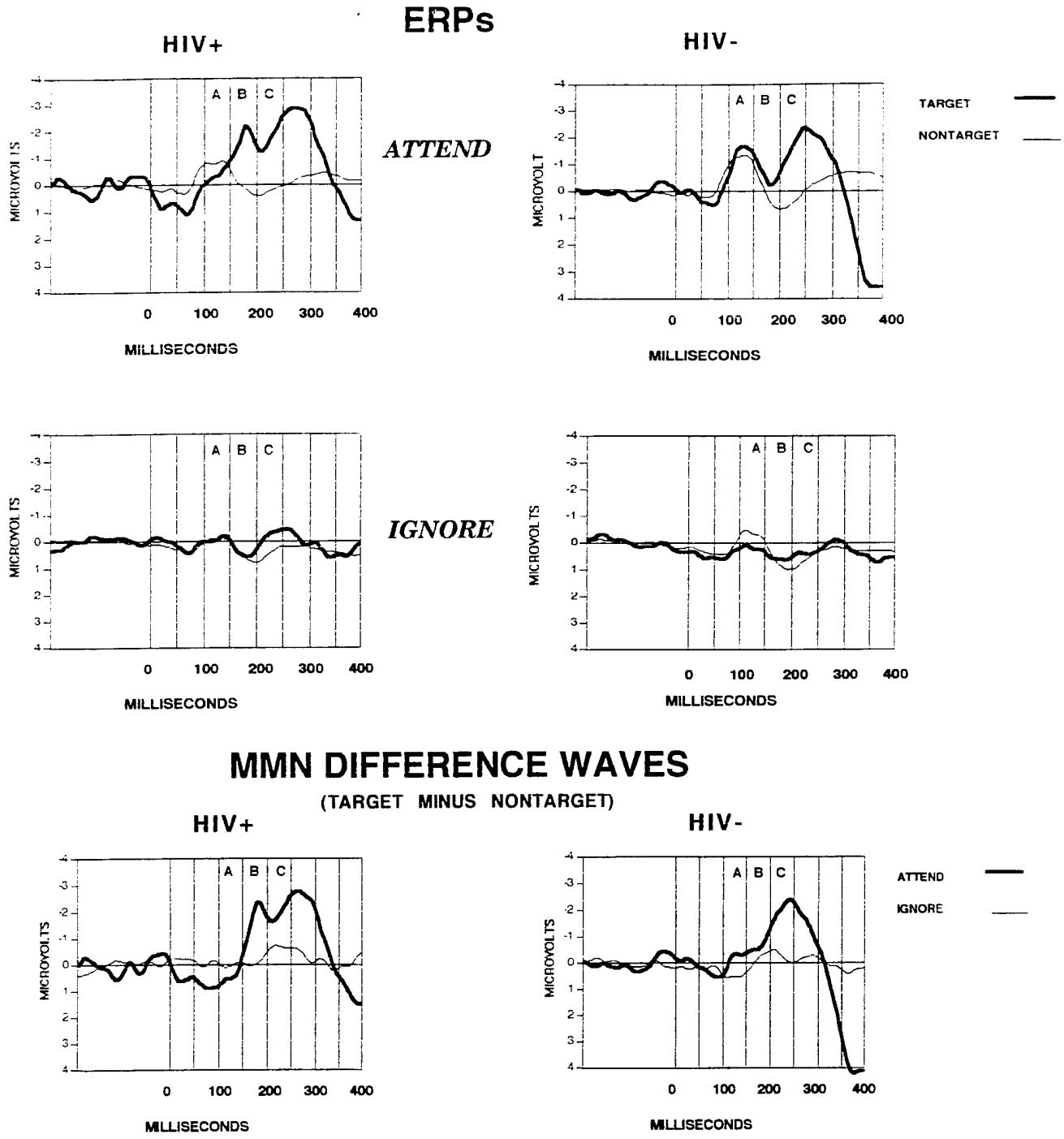

Figure 1.

Top panel: Grand average (N = 13/grp) ERPs for both HIV+ (left column) and HIV- (right column) groups recorded from midline scalp site Cz in response to dual oddball target and nontarget stimuli as a function of direction of attention. The mismatch negativity (MMN) is the region between 100 ms to 300 ms for the ERPs elicited to target stimuli. *Bottom panel.* Grand average (N = 13/grp) "Attend" and "Ignore" MMN difference waves (target ERP minus nontarget ERP) for both HIV+ (left column) and HIV- (right column) groups at midline scalp site Cz in response to attended versus ignored sequences of stimuli. *Note*: Statistical analyses performed over three successive 50-ms periods (A,B,C).

Table 2. ERP Grand Mean Amplitudes (μV) and Standard Error (±SE)

Window A (100-150 ms)

	HIV+ (N = 13)			HIV- (N = 13)		
	Fz	Cz	Pz	Fz	Cz	Pz
	Mean SE	Mean SE	Mean SE	Mean SE	Mean SE	Mean SE
Attend						
Targets	0.11 ±0.41	-0.23 ±0.35	-0.06 ±0.40	-0.75 ±0.38	-1.19 ±0.32	-0.81 ±0.27
Nontargets	-0.73 ±0.19	-0.81 ±0.19	-0.24 ±0.11	-0.95 ±0.19	-1.17 ±0.19	-0.59 ±0.11
Ignore						
Targets	0.13 ±0.25	-0.05 ±0.28	-0.08 ±0.26	0.41 ±0.21	0.14 ±0.22	0.16 ±0.28
Nontargets	0.14 ±0.08	-0.06 ±0.08	-0.03 ±0.07	-0.14 ±0.10	-0.36 ±0.11	-0.14 ±0.07

Window B (150-200 ms)

	HIV+ (N = 13)			HIV- (N = 13)		
	Fz	Cz	Pz	Fz	Cz	Pz
	Mean SE	Mean SE	Mean SE	Mean SE	Mean SE	Mean SE
Attend						
Targets	-1.17 ±0.53	-1.42 ±0.40	-0.78 ±0.56	-0.87 ±0.36	-0.90 ±0.32	-0.84 ±0.29
Nontargets	-0.35 ±0.14	-0.24 ±0.12	-0.15 ±0.09	-0.45 ±0.12	-0.43 ±0.12	-0.24 ±0.08
Ignore						
Targets	0.48 ±0.13	0.24 ±0.17	-0.28 ±0.26	0.65 ±0.22	0.45 ±0.17	0.25 ±0.19
Nontargets	0.40 ±0.14	0.28 ±0.14	-0.28 ±0.26	0.44 ±0.10	0.36 ±0.11	0.17 ±0.07

Window C (200-250 ms)

	HIV+ (N = 13)			HIV- (N = 13)		
	Fz	Cz	Pz	Fz	Cz	Pz
	Mean SE	Mean SE	Mean SE	Mean SE	Mean SE	Mean SE
Attend						
Targets	-1.28 ±0.56	-1.64 ±0.67	-1.03 ±0.56	-1.02 ±0.49	-1.16 ±0.49	-0.92 ±0.31
Nontargets	0.14 ±0.14	0.28 ±0.10	-0.03 ±0.08	0.26 ±0.13	0.51 ±0.12	0.15 ±0.09
Ignore						
Targets	0.28 ±0.23	0.02 ±0.26	-0.39 ±0.27	0.49 ±0.16	0.43 ±0.17	0.09 ±0.29
Nontargets	0.70 ±0.12	0.58 ±0.09	0.16 ±0.07	0.93 ±0.13	0.78 ±0.12	0.29 ±0.08

Table 3. MMN Difference Grand Mean Amplitudes (μV) and Standard Error (±SE)

	Window A (100-150 ms)					
	HIV+ (N = 13)			HIV- (N = 13)		
	Fz	Cz	Pz	Fz	Cz	Pz
	Mean SE	Mean SE	Mean SE	Mean SE	Mean SE	Mean SE
Attend	0.82 ±0.44	0.54 ±0.42	0.24 ±0.46	0.15 ±0.34	-0.08 ±0.29	-0.32 ±0.29
Ignore	-0.02 ±0.24	0.01 ±0.29	-0.05 ±0.28	0.58 ±0.17	0.51 ±0.16	0.27 ±0.25

	Window B (150-200 ms)					
	HIV+ (N = 13)			HIV- (N = 13)		
	Fz	Cz	Pz	Fz	Cz	Pz
	Mean SE	Mean SE	Mean SE	Mean SE	Mean SE	Mean SE
Attend	-1.10 ±0.46	-1.45 ±0.46	-0.83 ±0.58	-0.45 ±0.33	-0.54 ±0.27	-0.54 ±0.24
Ignore	0.20 ±0.20	-0.06 ±0.20	-0.37 ±0.26	0.09 ±0.18	0.00 ±0.15	0.06 ±0.17

	Window C (200-250 ms)					
	HIV+ (N = 13)			HIV- (N = 13)		
	Fz	Cz	Pz	Fz	Cz	Pz
	Mean SE	Mean SE	Mean SE	Mean SE	Mean SE	Mean SE
Attend	-1.44 ±0.59	-1.99 ±0.72	-0.93 ±0.57	-1.40 ±0.56	-1.92 ±0.56	-1.24 ±0.38
Ignore	-0.47 ±0.28	-0.63 ±0.29	-0.57 ±0.28	-0.33 ±0.14	-0.28 ±0.17	-0.17 ±0.28

Table 4. ERP Results

		Window A (100-150 ms)
	Result	**F-Statistic**
Attend	Group	$F(1,24) = 5.63$*
	Site	$F(1,24) = 4.58$*
Ignore	Site	$F(1,24) = 7.56$*
		Window B (150-200 ms)
	Result	**F-Statistic**
Attend	Tone	$F(1,24) = 18.35$**
Ignore	Site	$F(1,24) = 12.73$**
		Window C (200-250 ms)
	Result	**F-Statistic**
Attend	Tone	$F(1,24) = 16.39$**
Ignore	Site	$F(1,24) = 18.91$**

Table 5. MMN Difference (target minus nontarget) Results

	Window A (100-150 ms)
Result	**F-Statistic**
Group x Attention	$F(1,24) = 4.33$*
	Window B (150-200 ms)
Result	**F-Statistic**
Attention	$F(1,24) = 11.30$**
	Window C (200-250 ms)
Result	**F-Statistic**
Attention	$F(1,24) = 8.09$**

Note: All Site main effects underwent Geisser-Greenhouse correction in degrees of freedom.

* $p < .05$

** $p < .01$

Window B (150-200 ms). The analysis of mean amplitude measures from the Attend condition in Window B produced a main effect for Tone. The analysis indicated greater negativity in the mean amplitude measures to target tones in this latency window compared to nontarget tones (Table 2). Figure 1 (top panel) shows the augmented MMN elicited by both the HIV+ group and the HIV- group in this latency window. Although Figure 1 (top panel) shows a bifarcation in the MMN which could be a delayed N100, there were no significant group differences in this window indicating high variability in this region. The ANOVA of the mean amplitude measures from the Ignore condition in this latency window resulted in only a main effect for electrode Sites that is noted in Table 4.

Window C (200-250 ms). The analysis of mean amplitude measures from the Attend condition in Window C produced a main effect for Tone, indicating greater negativity in the mean amplitude measures in this latency window to the target tones compared to the nontarget tones (Table 2). Figure 1 (top panel) illustrates augmented N200 components of the MMN in this region by both the HIV+ and HIV- group compared to the attended nontargets. The ANOVA of the mean amplitude measures from the Ignore condition in this latency window resulted in only a main effect for electrode Sites that is noted in Table 4.

MMN Difference Results

Window A (100-150 ms). The analysis of the difference mean amplitude measures in Window A produced a main effect for electrode Site and a Group x Attention interaction (Table 5). The *t*-test pairwise comparisons of the interaction indicated both between-group and within-group differences in the mean amplitude measures in the interaction. The between-group differences indicated a greater negativity in the mean amplitude measures from the Attend condition for the HIV- group in comparison to the HIV+ group and greater negativity in the mean amplitude measures from the Ignore condition for the HIV+ group in comparison to the HIV- group (Table 3). Figure 1 (bottom panel) shows the two groups differ in this latency window in the Attend MMN difference wave and in the Ignore MMN difference wave. The within-group results indicated a difference between attentional conditions which is displayed in Figure 1 (bottom panel).

Window B (150-200 ms). The analysis of the difference mean amplitude measures in Window B produced a main effect for Attention indicating greater negativity in the mean amplitude measures in this latency window from the Attend condition compared to the Ignore condition (Table 5). Figure 1 (bottom panel) shows augmented Attend MMN difference waveforms for both groups in this latency window.

Window C (200-250 ms). The analysis of the difference mean amplitude measures in Window C produced a main effect for Attention (Table 5). These results, similar to those in Window B, indicated greater negativity in the mean amplitude measures from the Attend condition (Table 3). Figure 1 (bottom panel) shows augmented Attend MMN difference waveforms for both groups in this latency window.

DISCUSSION

The purpose of this report was to determine whether HIV-infected individuals demonstrated underlying neurological differences in perceptual processing. The results indicate that the 100-ms region of the Attend MMN in the HIV+ group was morphologically different from the HIV- group. The finding suggests that HIV affects neural processes critical to the detection of acoustical mismatch in a series of rapid auditory stimuli. The individuals tested in this study were healthy and functional [20], and owing to the absence of clinical manifestations, were considered to be in the early stages of the disease. However, it appears that HIV subtly affects the most basic processes in the central nervous system prior to the appearance of opportunistic infections and other overt symptoms of the disease. Furthermore, the HIV- group results replicated those reported by Woldorff et al. [25]. That is, augmented MMN waveforms and the underlying components were produced during the Attend condition to target tones, and no MMN waveforms were produced during the Ignore condition. Thus we conclude that our findings are genuine. In addition, while sampling procedures did not allow matching the experimental groups by race, there was no indication in the literature of systematic racial affects on ERPs. In future research, however, subject groups should be match by race if possible.

We are also confident that HIV alone and not intravenous (IV) drug use altered the MMN. Our sample of subjects were active-duty Navy or Marine Corps personnel, and therefore, subject to Naval regulations concerning screening for substance abuse [34]. This regulation requires that military personnel submit to monthly, random drug-urinalysis testing. This requirement ensures that members stay drug free at all times. Therefore, it is very unlikely that the HIV+ subjects evaluated in this study obtained HIV infection through IV drug use.

Reports on the source location for the magnetic counterparts to the 100-ms, N100 component (N100m), the MMN (mismatch field; MMF), and the magnetic correlate to optimized attentional focus in a dual oddball task (magnetic negative difference; Ndm), indicate they are elicited by neural activity in the supratemporal auditory cortex [35-36]. The MMF and Ndm sources were reported to be significantly more anterior in this region to N100m sources produced to all tones

[34-35]. The clear separation of the MMF and Ndm from the N100m suggests additional neural activity is involved in detecting acoustical deviancy in a stream of meaningful information. Our results suggest that HIV could compromise these underlying mechanisms in the early stages of the infection.

Only one other study has examined the MMN in HIV patients [37]. The study's methodology included a single oddball (20% oddball) paradigm at a delivery rate of approximately 1 tone/sec with subjects instructed to ignore the deliveries. They reported no significant HIV-related differences in the morphology of the waveforms in subgroups of asymptomatic and symptomatic HIV+ IV drug users compared to HIV- IV drug users. Thus, the single oddball procedure may not be as useful in monitoring HIV differences in the MMN as the rapid, dual oddball procedure.

In conclusion, it appears that HIV alters the neural generators that direct attention towards sensory information. In time as the disease progresses, HIV may produce a cumulative deficit in attention that becomes manifest in behavior and performance. Our results from this report and our earlier findings [20] suggest that the rapid (3/sec), dual, auditory oddball task may be a useful tool in monitoring HIV-related neuropathology and its affect on perceptual and cognitive processing.

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Thirteen asymptomatic HIV-infected (HIV+) and 13 healthy control (HIV-) subjects were instructed to detect "oddball" target tones from among a sequence of nontarget tones delivered rapidly (3 tones/sec) in one ear while ignoring a similar sequence delivered simultaneously in the opposite ear. Event-related potentials (ERPs) to all stimuli were recorded from midline scalp sites. Both groups produced ERP correlates, termed the mismatch negativity (MMN), to the oddball tones during delivery. However, the HIV+ group produced MMNs that were different in morphology to the HIV- group, suggesting that HIV may alter attentional perceptual processing. These results suggested that auditory ERPs elicited by rapid, dichotic stimulus presentations may be useful tools in monitoring subclinical effects of HIV-related neuropathology on perceptual processing.

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